SEQUENCE LISTING

<110> Walsh, Christopher
     Chao, Hengjun
     Burstein, Haim
     Lynch, Carmel
     Stepan, Tony
     Munson, Keith

<120> Adeno-Associated Virus Vectors Encoding Factor VIII and
 Methods of Using Same

<130> 35052/204375

<140> US 09/689,430
<141> 2000-10-12

<150> 60/158,780
<151> 1999-10-12

<160> 5

<170> FastSEQ for Windows Version 4.0

<210> 1
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<212> DNA
<213> Artificial Sequence

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<221> CDS
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atg caa ata gag ctc tcc acc tgc ttc ttt ctg tgc ctt ttg cga ttc 467
Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
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tgc ttt agt gcc acc aga aga tac tac ctg ggt gca gtg gaa ctg tca 515
Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
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tgg gac tat atg caa agt gat ctc ggt gag ctg cct gtg gac gca aga 563
Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg
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Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
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tac aaa aag act ctg ttt gta gaa ttc acg gtt cac ctt ttc aac atc      659
Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile
65                  70                  75                      80

gct aag cca agg cca ccc tgg atg ggt ctg cta ggt cct acc atc cag      707
Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85                  90                  95

gct gag gtt tat gat aca gtg gtc att aca ctt aag aac atg gct tcc      755
Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser
            100                 105                 110

cat cct gtc agt ctt cat gct gtt ggt gta tcc tac tgg aaa gct tct      803
His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
            115                 120                 125

gag gga gct gaa tat gat gat cag acc agt caa agg gag aaa gaa gat      851
Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
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gat aaa gtc ttc cct ggt gga agc cat aca tat gtc tgg cag gtc ctg      899
Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

aaa gag aat ggt cca atg gcc tct gac cca ctg tgc ctt acc tac tca      947
Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

tat ctt tct cat gtg gac ctg gta aaa gac ttg aat tca ggc ctc att      995
Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

gga gcc cta cta gta tgt aga gaa ggg agt ctg gcc aag gaa aag aca     1043
Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
            195                 200                 205

cag acc ttg cac aaa ttt ata cta ctt ttt gct gta ttt gat gaa ggg     1091
Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

aaa agt tgg cac tca gaa aca aag aac tcc ttg atg cag gat agg gat     1139
Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

gct gca tct gct cgg gcc tgg cct aaa atg cac aca gtc aat ggt tat     1187
Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
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gta aac agg tct ctg cca ggt ctg att gga tgc cac agg aaa tca gtc     1235
Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
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2

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tat tgg cat gtg att gga atg ggc acc act cct gaa gtg cac tca ata    1283
Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
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ttc ctc gaa ggt cac aca ttt ctt gtg agg aac cat cgc cag gcg tcc    1331
Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
        290               295               300

ttg gaa atc tcg cca ata act ttc ctt act gct caa aca ctc ttg atg    1379
Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305               310               315               320

gac ctt gga cag ttt cta ctg ttt tgt cat atc tct tcc cac caa cat    1427
Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
            325               330               335

gat ggc atg gaa gct tat gtc aaa gta gac agc tgt cca gag gaa ccc    1475
Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340               345               350

caa cta cga atg aaa aat aat gaa gaa gcg gaa gac tat gat gat gat    1523
Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
            355               360               365

ctt act gat tct gaa atg gat gtg gtc agg ttt gat gat gac aac tct    1571
Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
370               375               380

cct tcc ttt atc caa att cgc tca gtt gcc aag aag cat cct aaa act    1619
Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385               390               395               400

tgg gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc    1667
Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405               410               415

tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac    1715
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420               425               430

aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg    1763
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
            435               440               445

gca tac aca gat gaa acc ttt aag act cgt gaa gct att cag cat gaa    1811
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
            450               455               460

tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg    1859
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465               470               475               480

ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct    1907
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
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3

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cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa    1955
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500             505             510

ggt gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc    2003
Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
            515             520             525

aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat    2051
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
            530             535             540

cct cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga    2099
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545             550             555             560

gat cta gct tca gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa    2147
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
            565             570             575

tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc    2195
Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580             585             590

atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag    2243
Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
            595             600             605

aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat    2291
Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
            610             615             620

cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt    2339
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625             630             635             640

ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg    2387
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
            645             650             655

tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc    2435
Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660             665             670

tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc    2483
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
            675             680             685

cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca    2531
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
            690             695             700

ggt cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc    2579
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705             710             715             720
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4

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atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat          2627
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
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tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa          2675
Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
                740                     745                 750

aac aat gcc att gaa cca aga agc ttc tcc cag aat tca aga cac cct          2723
Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro
                755                     760                 765

agc act agg caa aag caa ttt aat gcc acc cca cca gtc ttg aaa cgc          2771
Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Pro Pro Val Leu Lys Arg
    770                     775                 780

cat caa cgg gaa ata act cgt act act ctt cag tca gat caa gag gaa          2819
His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu
785                     790                     795                 800

att gac tat gat gat acc ata tca gtt gaa atg aag aag gaa gat ttt          2867
Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe
                805                     810                 815

gac att tat gat gag gat gaa aat cag agc ccc cgc agc ttt caa aag          2915
Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys
                820                     825                 830

aaa aca cga cac tat ttt att gct gca gtg gag agg ctc tgg gat tat          2963
Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr
                835                     840                 845

ggg atg agt agc tcc cca cat gtt cta aga aac agg gct cag agt ggc          3011
Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly
    850                     855                 860

agt gtc cct cag ttc aag aaa gtt gtt ttc cag gaa ttt act gat ggc          3059
Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly
865                     870                     875                 880

tcc ttt act cag ccc tta tac cgt gga gaa cta aat gaa cat ttg gga          3107
Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly
                885                     890                 895

ctc ctg ggg cca tat ata aga gca gaa gtt gaa gat aat atc atg gta          3155
Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val
                900                     905                 910

act ttc aga aat cag gcc tct cgt ccc tat tcc ttc tat tct agc ctt          3203
Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu
                915                     920                 925

att tct tat gag gaa gat cag agg caa gga gca gaa cct aga aaa aac          3251
Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn
    930                     935                 940
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5

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ttt gtc aag cct aat gaa acc aaa act tac ttt tgg aaa gtg caa cat       3299
Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His
945                 950                 955                 960

cat atg gca ccc act aaa gat gag ttt gac tgc aaa gcc tgg gct tat       3347
His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr
                965                 970                 975

ttc tct gat gtt gac ctg gaa aaa gat gtg cac tca ggc ctg att gga       3395
Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly
                980                 985                 990

ccc ctt ctg gtc tgc cac act aac aca ctg aac cct gct cat ggg aga       3443
Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg
                995                 1000                1005

caa gtg aca gta cag gaa ttt gct ctg ttt ttc acc atc ttt gat gag       3491
Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu
    1010                1015                1020

acc aaa agc tgg tac ttc act gaa aat atg gaa aga aac tgc agg gct       3539
Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala
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ccc tgc aat atc cag atg gaa gat ccc act ttt aaa gag aat tat cgc       3587
Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg
                1045                1050                1055

ttc cat gca atc aat ggc tac ata atg gat aca cta cct ggc tta gta       3635
Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val
                1060                1065                1070

atg gct cag gat caa agg att cga tgg tat ctg ctc agc atg ggc agc       3683
Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser
    1075                1080                1085

aat gaa aac atc cat tct att cat ttc agt gga cat gtg ttc act gta       3731
Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val
    1090                1095                1100

cga aaa aaa gag gag tat aaa atg gca ctg tac aat ctc tat cca ggt       3779
Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly
1105                1110                1115                1120

gtt ttt gag aca gtg gaa atg tta cca tcc aaa gct gga att tgg cgg       3827
Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg
                1125                1130                1135

gtg gaa tgc ctt att ggc gag cat cta cat gct ggg atg agc aca ctt       3875
Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu
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ttt ctg gtg tac agc aat aag tgt cag act ccc ctg gga atg gct tct       3923
Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser
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6

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gga cac att aga gat ttt cag att aca gct tca gga caa tat gga cag        3971
Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln
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tgg gcc cca aag ctg gcc aga ctt cat tat tcc gga tca atc aat gcc        4019
Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala
1185            1190                1195                1200

tgg agc acc aag gag ccc ttt tct tgg atc aag gtg gat ctg ttg gca        4067
Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala
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cca atg att att cac ggc atc aag acc cag ggt gcc cgt cag aag ttc        4115
Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe
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tcc agc ctc tac atc tct cag ttt atc atc atg tat agt ctt gat ggg       4163
Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly
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aag aag tgg cag act tat cga gga aat tcc act gga acc tta atg gtc        4211
Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val
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ttc ttt ggc aat gtg gat tca tct ggg ata aaa cac aat att ttt aac       4259
Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn
1265                1270                1275                1280

cct cca att att gct cga tac atc cgt ttg cac cca act cat tat agc        4307
Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser
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att cgc agc act ctt cgc atg gag ttg atg ggc tgt gat tta aat agt        4355
Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser
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tgc agc atg cca ttg gga atg gag agt aaa gca ata tca gat gca cag       4403
Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln
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att act gct tca tcc tac ttt acc aat atg ttt gcc acc tgg tct cct        4451
Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro
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Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro
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cag gtg aat aat cca aaa gag tgg ctg caa gtg gac ttc cag aag aca        4547
Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr
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atg aaa gtc aca gga gta act act cag gga gta aaa tct ctg ctt acc       4595
Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr
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7

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cag tgg act ctc ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga    4691
Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly
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aat caa gac tcc ttc aca cct gtg gtg aac tct cta gac cca ccg tta    4739
Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu
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ctg act cgc tac ctt cga att cac ccc cag agt tgg gtg cac cag att    4787
Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile
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gcc ctg agg atg gag gtt ctg ggc tgc gag gca cag gac ctc tac tga    4835
Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr  *
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8

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cagatgcgta aggagaaaat accgcatcag gaaattgtaa acgttaatat tttgttaaaa 7415
ttcgcgttaa attttttgtta aatcagctca ttttttaacc aataggccga aatcggcaaa 7475
atcccttata aatcaaaaga atagaccgag atagggttga gtgttgttcc agtttggaac 7535
aagagtccac tattaaagaa cgtggactcc aacgtcaaag ggcgaaaaac cgtctatcag 7595
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aaagcactaa atcggaaccc taaagggagc ccccgattta gagcttgacg gggaaagccg 7715
gcgaacgtgg cgagaaagga agggaagaaa gcgaaaggag cgggcgctag ggcgctggca 7775
agtgtagcgg tcacgctgcg cgtaaccacc acacccgccg cgcttaatgc gccgctacag 7835
ggcgcgtcgc gccattcgcc attcaggcta cgcaactgtt gggaagggcg atcggtgcgg 7895
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<213> Homo sapiens B-domain deleted factor VIII

<220>
<223> Homo sapiens BDD FVIII

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
 1               5                  10                  15
Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
            20                  25                  30
Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg
        35                  40                  45
Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
    50                  55                  60
Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile
65                  70                  75                  80
Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
            85                  90                  95
Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser
        100                 105                 110
His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125
Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140
Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160
Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
            165                 170                 175
Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
        180                 185                 190
Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205
Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220
Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240
```
                                9

```
Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
            245             250                 255
Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260             265                 270
Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
    275                 280                 285
Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300
Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320
Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335
Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350
Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
            355                 360                 365
Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380
Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400
Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
            435                 440                 445
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510
Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
            515                 520                 525
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575
Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590
Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
            595                 600                 605
Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655
Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
            675                 680                 685
```

10

```
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695             700
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710             715                 720
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725             730             735
Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740             745             750
Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro
        755             760             765
Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Pro Pro Val Leu Lys Arg
    770             775             780
His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu
785             790             795                 800
Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe
            805             810             815
Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys
        820             825             830
Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr
    835             840             845
Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly
    850             855             860
Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly
865             870             875                 880
Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly
            885             890             895
Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val
            900             905             910
Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu
    915             920             925
Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn
    930             935             940
Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His
945             950             955                 960
His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr
            965             970             975
Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly
            980             985             990
Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg
        995             1000            1005
Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu
    1010            1015            1020
Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala
1025            1030            1035                1040
Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg
                1045            1050            1055
Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val
            1060            1065            1070
Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser
        1075            1080            1085
Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val
    1090            1095            1100
Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly
1105            1110            1115                1120
Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg
            1125            1130            1135
```
11

Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu
      1140   1145   1150
Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser
      1155   1160   1165
Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln
    1170   1175   1180
Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala
1185   1190   1195   1200
Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala
              1205   1210   1215
Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe
            1220   1225   1230
Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly
      1235   1240   1245
Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val
    1250   1255   1260
Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn
1265   1270   1275   1280
Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser
            1285   1290   1295
Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser
            1300   1305   1310
Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln
      1315   1320   1325
Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro
      1330   1335   1340
Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro
1345   1350   1355   1360
Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr
            1365   1370   1375
Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr
            1380   1385   1390
Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His
      1395   1400   1405
Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly
    1410   1415   1420
Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu
1425   1430   1435   1440
Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile
            1445   1450   1455
Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
        1460   1465   1470

<210> 3
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     VIII

<221> CDS
<222> (435)...(4730)

12

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gacgcccggg ctttgcccgg gcggcctcag tgagcgagcg agcgcgcaga gagggagtgg 120
ccaactccat cactaggggt tcctcagatc tctttctaag taaacagtac atgaaccttt 180
accccgttgc tcggcaacgg cctggtctgt gccaagtgtt tgctgacgca acccccactg 240
gctggggctt ggccataggc catcagcgca tgcggatctc agtgtggttt tgcaagagga 300
agcaaaaagc ctctccaccc aggcctggaa tgtttccacc caatgtcgag cagtgtggtt 360
ttgcaagagg aagcaaaaag cctctccacc caggcctgga ctcgacctcg agagtacttc 420
tagaaatacg agcc atg caa gta gag ctc tac acc tgc tgc ttt ctg tgc    470
               Met Gln Val Glu Leu Tyr Thr Cys Cys Phe Leu Cys
               1               5                   10
```

```
ctt ttg ccc ttc agc ctt agt gcc acc aga aaa tac tac ctc ggt gca    518
Leu Leu Pro Phe Ser Leu Ser Ala Thr Arg Lys Tyr Tyr Leu Gly Ala
        15                  20                  25
```

```
gtg gaa ctg tcc tgg gac tat atg caa agt gac ctg ctc agt gcg ctg    566
Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Leu Ser Ala Leu
    30                  35                  40
```

```
cac gcg gat aca agc ttt tct tcc agg gtg cca gga tct ttg cca ctc    614
His Ala Asp Thr Ser Phe Ser Ser Arg Val Pro Gly Ser Leu Pro Leu
45                  50                  55                  60
```

```
acc acg tca gtc acg tac aga aag act gtg ttt gta gag ttt aca gat    662
Thr Thr Ser Val Thr Tyr Arg Lys Thr Val Phe Val Glu Phe Thr Asp
            65                  70                  75
```

```
gac ctt ttc aac att gcc aag ccc agg cca ccg tgg atg ggc ctg ctg    710
Asp Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu
            80                  85                  90
```

```
ggt cct acc atc cag gct gag gtt tat gac aca gtg gtc att gtc ctt    758
Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Val Leu
            95                  100                 105
```

```
aag aac atg gct tct cat cct gtc agc ctt cac gct gtt ggt gta tcc    806
Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser
    110                 115                 120
```

```
tat tgg aaa gct tct gaa ggt gct gag tat gag gat cag acc agc caa    854
Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Glu Asp Gln Thr Ser Gln
125                 130                 135                 140
```

```
aag gag aag gaa gat gat aat gtc att cct ggt gaa agc cat acc tat    902
Lys Glu Lys Glu Asp Asp Asn Val Ile Pro Gly Glu Ser His Thr Tyr
                145                 150                 155
```

```
gtc tgg cag gtc ctg aaa gag aat ggc cca atg gcc tct gat cca cca    950
Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Pro
            160                 165                 170
```

```
tgt ctc acc tac tca tat ttt tca cac gtg gac ctg gtg aaa gac ctg    998
Cys Leu Thr Tyr Ser Tyr Phe Ser His Val Asp Leu Val Lys Asp Leu
        175                 180                 185
```

13

```
aat tca ggc ctc att gga gcc ctg ctg gtt tgc aaa gaa ggg agt ctg    1046
Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Lys Glu Gly Ser Leu
    190             195             200

gcc aaa gaa agg aca cag acc ttg cag gaa ttt gtc cta ctt ttt gct    1094
Ala Lys Glu Arg Thr Gln Thr Leu Gln Glu Phe Val Leu Leu Phe Ala
205             210             215             220

gta ttt gat gaa ggg aaa agt tgg cac tca gaa aca aat gcg tct ttg    1142
Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Asn Ala Ser Leu
                225             230             235

aca cag gct gag gcc cag cat gag ctg cac acc atc aat ggc tat gta    1190
Thr Gln Ala Glu Ala Gln His Glu Leu His Thr Ile Asn Gly Tyr Val
            240             245             250

aac agg tct ctg cca ggt ctt act gtg tgt cac aag aga tca gtc tat    1238
Asn Arg Ser Leu Pro Gly Leu Thr Val Cys His Lys Arg Ser Val Tyr
        255             260             265

tgg cat gtg att gga atg ggc acc acc ccc gaa gtg cac tca att ttt    1286
Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe
    270             275             280

ctc gaa ggt cac aca ttt ctt gtg agg aac cac cgc cag gcc tcc ttg    1334
Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu
285             290             295             300

gag atc tca cca att act ttc ctt act gct cag aca ttc ctg atg gac    1382
Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Phe Leu Met Asp
                305             310             315

ctt ggc cag ttt cta ctg ttt tgt cat atc cct tcc cat caa cat gat    1430
Leu Gly Gln Phe Leu Leu Phe Cys His Ile Pro Ser His Gln His Asp
            320             325             330

ggt atg gaa gct tat gtc aaa gta gat agc tgc cca gag gaa ccc cag    1478
Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln
            335             340             345

ctg cgc atg aaa aat aat gaa gat aaa gat tat gat gat ggt ctt tat    1526
Leu Arg Met Lys Asn Asn Glu Asp Lys Asp Tyr Asp Asp Gly Leu Tyr
    350             355             360

gat tct gac atg gac gta gtt agc ttt gat gac gac agc tct tct ccc    1574
Asp Ser Asp Met Asp Val Val Ser Phe Asp Asp Asp Ser Ser Ser Pro
365             370             375             380

ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act tgg gtc    1622
Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val
                385             390             395

cac tat att gct gct gag gag gag gac tgg gac tat gct ccc tca ggc    1670
His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Ser Gly
            400             405             410
```

14

```
ccc acc ccc aat gat aga agt cat aaa aat ctg tat ttg aac aat ggt     1718
Pro Thr Pro Asn Asp Arg Ser His Lys Asn Leu Tyr Leu Asn Asn Gly
        415                 420                 425

cct cag cgg att ggt aag aag tac aaa aaa gtc cga ttt gtg gca tac     1766
Pro Gln Arg Ile Gly Lys Lys Tyr Lys Lys Val Arg Phe Val Ala Tyr
        430                 435                 440

aca gat gag aca ttt aag act cgt gaa gct att cag tat gaa tca gga     1814
Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln Tyr Glu Ser Gly
445                 450                 455                 460

atc ctg gga cct tta ctt tat gga gaa gtt gga gac aca ctg ctg att     1862
Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile
                465                 470                 475

ata ttt aag aat caa gcc agc cgg cca tat aac atc tac cct cat ggg     1910
Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly
                480                 485                 490

atc aat tat gtc act cct ctg cac aca ggg aga ttg cca aaa ggt gtg     1958
Ile Asn Tyr Val Thr Pro Leu His Thr Gly Arg Leu Pro Lys Gly Val
                495                 500                 505

aaa cat ttg aaa gat atg cca att ctg ccg gga gag ata ttc aag tat     2006
Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr
        510                 515                 520

aaa tgg aca gtg acc gta gaa gat gga cca act aaa tca gat cct cgg     2054
Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg
525                 530                 535                 540

tgc ctg acc cga tat tac tca agc ttc att aat ctg gag aga gat cta     2102
Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Ile Asn Leu Glu Arg Asp Leu
                545                 550                 555

gct tca gga ctc att ggc cct ctt ctc atc tgc tac aaa gaa tct gta     2150
Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val
                560                 565                 570

gat caa aga gga aac cag atg atg tca gac aag aga aat gtc atc ctg     2198
Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val Ile Leu
        575                 580                 585

ttt tct gta ttt gat gag aat cga agc tgg tac ctc aca gag aat atg     2246
Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Met
        590                 595                 600

cag cgc ttc ctc ccc aat gca gat gta gtg cag ccc cat gac cca gag     2294
Gln Arg Phe Leu Pro Asn Ala Asp Val Val Gln Pro His Asp Pro Glu
605                 610                 615                 620

ttc caa ctc tct aac atc atg cac agc atc aat ggc tat gtt ttt gac     2342
Phe Gln Leu Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp
                625                 630                 635
```

15

```
aac ttg cag ctg tca gtt tgt ttg cat gag gtg gcg tac tgg tac att   2390
Asn Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile
        640             645             650

cta agt gtt gga gca caa act gac ttc ctg tct gtc ttc ttc tct gga   2438
Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly
        655             660             665

tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctt acc ctc ttc   2486
Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe
    670             675             680

cca ttc tca gga gaa act gtc ttc atg tca atg gaa aac cca ggt ctg   2534
Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu
685             690             695             700

tgg gtt ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc atg aca   2582
Trp Val Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr
            705             710             715

gcc tta ctg aag gtt tct agt tgt aac agg aac att gat gat tat tat   2630
Ala Leu Leu Lys Val Ser Ser Cys Asn Arg Asn Ile Asp Asp Tyr Tyr
        720             725             730

gag gac aca tac gaa gat att cca act ccc ctg cta aat gaa aac aat   2678
Glu Asp Thr Tyr Glu Asp Ile Pro Thr Pro Leu Leu Asn Glu Asn Asn
        735             740             745

gta att aaa cct aga agc ttc tcc cag aat tca agg cac cct agc act   2726
Val Ile Lys Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro Ser Thr
    750             755             760

aag gaa aag caa ttg aaa atg aag aga gaa gat ttt gac atc tac ggc   2774
Lys Glu Lys Gln Leu Lys Met Lys Arg Glu Asp Phe Asp Ile Tyr Gly
765             770             775             780

gac tat gaa aat cag ggc ctc cgc agc ttt caa aag aaa aca cga cac   2822
Asp Tyr Glu Asn Gln Gly Leu Arg Ser Phe Gln Lys Lys Thr Arg His
            785             790             795

tat ttc att gct gca gtg gag cgt ctc tgg gat tat ggg atg agt aga   2870
Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Arg
        800             805             810

tct ccc cat ata cta aga aac agg gct caa agt ggg gat gtc cag cag   2918
Ser Pro His Ile Leu Arg Asn Arg Ala Gln Ser Gly Asp Val Gln Gln
        815             820             825

ttc aag aag gtg gtt ttc cag gaa ttt act gat gga tcc ttt act cag   2966
Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln
    830             835             840

ccc tta tac cgt gga gaa ctg aat gaa cac ttg gga ctc ttg ggg cca   3014
Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro
845             850             855             860
```

16

```
tat ata aga gca gaa gtt gaa gac aat atc gtg gta act ttc aaa aac    3062
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Val Val Thr Phe Lys Asn
                865             870             875

cag gcc tct cgt ccc tac tcc ttc tat tct agt ctt att tct tat gac    3110
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Asp
                880             885             890

gaa gat gag gga caa gga gca gaa cct aga aga aag ttt gtc aac cct    3158
Glu Asp Glu Gly Gln Gly Ala Glu Pro Arg Arg Lys Phe Val Asn Pro
                895             900             905

aat gaa acc aaa att tac ttt tgg aaa gtg cag cat cat atg gca ccc    3206
Asn Glu Thr Lys Ile Tyr Phe Trp Lys Val Gln His His Met Ala Pro
        910             915             920

act aaa gat gag ttt gac tgc aaa gcc tgg gct tat ttt tct gat gtt    3254
Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val
925             930             935             940

gat ttg gag aaa gat gtg cac tca ggc ttg att gga ccc ctt ctg atc    3302
Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile
                945             950             955

tgc cgc agt aac aca ctg aac cct gct cat ggg aga caa gtg aca gtg    3350
Cys Arg Ser Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val
                960             965             970

cag gag ttt gcc ctg gtt ttc act ata ttc gat gag act aag agc tgg    3398
Gln Glu Phe Ala Leu Val Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp
                975             980             985

tac ttc act gaa aac ctg gaa agg aac tgt aga gct ccc tgc aat gtc    3446
Tyr Phe Thr Glu Asn Leu Glu Arg Asn Cys Arg Ala Pro Cys Asn Val
                990             995             1000

cag aag gag gac cct act cta aaa gaa aac ttc cgc ttc cat gca atc    3494
Gln Lys Glu Asp Pro Thr Leu Lys Glu Asn Phe Arg Phe His Ala Ile
1005            1010            1015            1020

aac ggc tat gtg aag gat aca ctc cct ggc tta gta atg gct cag gat    3542
Asn Gly Tyr Val Lys Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp
                1025            1030            1035

caa aag gtt cga tgg tat ctg ctc agc atg ggc agc aac gaa aac att    3590
Gln Lys Val Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile
                1040            1045            1050

cat tcc att cac ttc agt gga cat gtg ttc act gta cgg aaa aaa gag    3638
His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu
                1055            1060            1065

gaa tat aaa atg gca gtc tac aac ctc tat cca ggt gtt ttt gag act    3686
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr
        1070            1075            1080
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gtg gaa atg cta cca tcc caa gtt gga atc tgg cgg ata gaa tgc ctt      3734
Val Glu Met Leu Pro Ser Gln Val Gly Ile Trp Arg Ile Glu Cys Leu
1085                1090                1095                1100

atc ggc gag cac ctg caa gcc ggg atg agc act ctg ttt ctg gtg tac      3782
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Leu Phe Leu Val Tyr
                    1105                1110                1115

agc aag aag tgt cag act cca ctg ggg atg gct tcc gga cac att aga      3830
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg
                1120                1125                1130

gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag      3878
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys
            1135                1140                1145

ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag      3926
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys
            1150                1155                1160

gat ccc ttt tcc tgg atc aag gtg gat ctc ttg gca ccg atg att att      3974
Asp Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile
1165                1170                1175                1180

cac ggc atc atg acc cag ggg gcc cgc cag aag ttc tcc agc ctc tac      4022
His Gly Ile Met Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr
                    1185                1190                1195

gtg tct cag ttt atc atc atg tac agt ctg gat ggc aac aag tgg cac      4070
Val Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Asn Lys Trp His
                1200                1205                1210

agt tac cga ggg aat tcc acg ggg acc tta atg gtc ttc ttt ggc aac      4118
Ser Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn
            1215                1220                1225

gtg gat tca tct ggg atc aaa cac aat att ttt aac cct ccg att att      4166
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile
            1230                1235                1240

gct cag tac atc cgt ttg cac cca acc cat tac agc atc cgc agc act      4214
Ala Gln Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr
1245                1250                1255                1260

ctt cgc atg gag ctc ttg ggc tgt gac ttc aac agt tgc agc atg ccg      4262
Leu Arg Met Glu Leu Leu Gly Cys Asp Phe Asn Ser Cys Ser Met Pro
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ctg ggg atg gag agt aaa gca ata tca gat gct cag atc act gcc tcg      4310
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser
                1280                1285                1290

tcc tac cta agc agt atg ctt gcc act tgg tct cct tcc caa gcc cgg      4358
Ser Tyr Leu Ser Ser Met Leu Ala Thr Trp Ser Pro Ser Gln Ala Arg
            1295                1300                1305
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ctg cac ctg cag ggc agg act aat gcc tgg aga cct cag gca aat aac   4406
Leu His Leu Gln Gly Arg Thr Asn Ala Trp Arg Pro Gln Ala Asn Asn
    1310                1315                1320

cca aaa gag tgg ctg caa gtg gac ttc cgg aag acc atg aaa gtc aca   4454
Pro Lys Glu Trp Leu Gln Val Asp Phe Arg Lys Thr Met Lys Val Thr
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gga ata acc acc cag ggg gtg aaa tct ctc ctc atc agc atg tat gtg   4502
Gly Ile Thr Thr Gln Gly Val Lys Ser Leu Leu Ile Ser Met Tyr Val
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aag gag ttc ctc atc tcc agt agt caa gat ggc cat aac tgg act ctg   4550
Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Asn Trp Thr Leu
            1360                1365                1370

ttt ctt cag aat ggc aaa gtc aag gtc ttc cag gga aac cgg gac tcc   4598
Phe Leu Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Arg Asp Ser
            1375                1380                1385

tcc acg cct gtg cgg aac cgt ctc gaa ccc ccg ctg gtg gct cgc tac   4646
Ser Thr Pro Val Arg Asn Arg Leu Glu Pro Pro Leu Val Ala Arg Tyr
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gtg cgc ctg cac ccg cag agc tgg gcg cac cac atc gcc ctg agg ctg   4694
Val Arg Leu His Pro Gln Ser Trp Ala His His Ile Ala Leu Arg Leu
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gag gtc ctg ggc tgc gac acc cag cag ccc gcc tga cccgcgcctc        4740
Glu Val Leu Gly Cys Asp Thr Gln Gln Pro Ala  *
            1425                1430

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Trp Asp Tyr Met Gln Ser Asp Leu Leu Ser Ala Leu His Ala Asp Thr
        35                  40                  45
Ser Phe Ser Ser Arg Val Pro Gly Ser Leu Pro Leu Thr Thr Ser Val
    50                  55                  60
Thr Tyr Arg Lys Thr Val Phe Val Glu Phe Thr Asp Asp Leu Phe Asn
65                  70                  75                  80
Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
                85                  90                  95
Gln Ala Glu Val Tyr Asp Thr Val Val Ile Val Leu Lys Asn Met Ala
            100                 105                 110
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala
        115                 120                 125
Ser Glu Gly Ala Glu Tyr Glu Asp Gln Thr Ser Gln Lys Glu Lys Glu
    130                 135                 140
Asp Asp Asn Val Ile Pro Gly Glu Ser His Thr Tyr Val Trp Gln Val
145                 150                 155                 160
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Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Pro Cys Leu Thr Tyr
              165                 170                 175
Ser Tyr Phe Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
              180                 185                 190
Ile Gly Ala Leu Leu Val Cys Lys Glu Gly Ser Leu Ala Lys Glu Arg
              195                 200                 205
Thr Gln Thr Leu Gln Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
          210                 215                 220
Gly Lys Ser Trp His Ser Glu Thr Asn Ala Ser Leu Thr Gln Ala Glu
225                 230                 235                 240
Ala Gln His Glu Leu His Thr Ile Asn Gly Tyr Val Asn Arg Ser Leu
                  245                 250                 255
Pro Gly Leu Thr Val Cys His Lys Arg Ser Val Tyr Trp His Val Ile
              260                 265                 270
Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His
          275                 280                 285
Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro
      290                 295                 300
Ile Thr Phe Leu Thr Ala Gln Thr Phe Leu Met Asp Leu Gly Gln Phe
305                 310                 315                 320
Leu Leu Phe Cys His Ile Pro Ser His Gln His Asp Gly Met Glu Ala
                  325                 330                 335
Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys
              340                 345                 350
Asn Asn Glu Asp Lys Asp Tyr Asp Asp Gly Leu Tyr Asp Ser Asp Met
          355                 360                 365
Asp Val Val Ser Phe Asp Asp Asp Ser Ser Ser Pro Phe Ile Gln Ile
      370                 375                 380
Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala
385                 390                 395                 400
Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Ser Gly Pro Thr Pro Asn
                  405                 410                 415
Asp Arg Ser His Lys Asn Leu Tyr Leu Asn Asn Gly Pro Gln Arg Ile
              420                 425                 430
Gly Lys Lys Tyr Lys Lys Val Arg Phe Val Ala Tyr Thr Asp Glu Thr
              435                 440                 445
Phe Lys Thr Arg Glu Ala Ile Gln Tyr Glu Ser Gly Ile Leu Gly Pro
      450                 455                 460
Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn
465                 470                 475                 480
Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Asn Tyr Val
                  485                 490                 495
Thr Pro Leu His Thr Gly Arg Leu Pro Lys Gly Val Lys His Leu Lys
              500                 505                 510
Asp Met Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val
      515                 520                 525
Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg
      530                 535                 540
Tyr Tyr Ser Ser Phe Ile Asn Leu Glu Arg Asp Leu Ala Ser Gly Leu
545                 550                 555                 560
Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly
              565                 570                 575
Asn Gln Met Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe
              580                 585                 590
Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Met Gln Arg Phe Leu
      595                 600                 605
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Pro Asn Ala Asp Val Val Gln Pro His Asp Pro Glu Phe Gln Leu Ser
    610   615   620
Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Asn Leu Gln Leu
625   630   635   640
Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Val Gly
                645   650   655
Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys
                660   665   670
His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly
            675   680   685
Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Val Leu Gly
        690   695   700
Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys
705   710   715   720
Val Ser Ser Cys Asn Arg Asn Ile Asp Asp Tyr Tyr Glu Asp Thr Tyr
                725   730   735
Glu Asp Ile Pro Thr Pro Leu Leu Asn Glu Asn Asn Val Ile Lys Pro
                740   745   750
Arg Ser Phe Ser Gln Asn Ser Arg His Pro Ser Thr Lys Glu Lys Gln
            755   760   765
Leu Lys Met Lys Arg Glu Asp Phe Asp Ile Tyr Gly Asp Tyr Glu Asn
    770   775   780
Gln Gly Leu Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala
785   790   795   800
Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Arg Ser Pro His Ile
                805   810   815
Leu Arg Asn Arg Ala Gln Ser Gly Asp Val Gln Gln Phe Lys Lys Val
            820   825   830
Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg
            835   840   845
Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala
    850   855   860
Glu Val Glu Asp Asn Ile Val Val Thr Phe Lys Asn Gln Ala Ser Arg
865   870   875   880
Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Asp Glu Asp Glu Gly
                885   890   895
Gln Gly Ala Glu Pro Arg Arg Lys Phe Val Asn Pro Asn Glu Thr Lys
            900   905   910
Ile Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu
        915   920   925
Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys
    930   935   940
Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Arg Ser Asn
945   950   955   960
Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala
                965   970   975
Leu Val Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu
                980   985   990
Asn Leu Glu Arg Asn Cys Arg Ala Pro Cys Asn Val Gln Lys Glu Asp
            995   1000   1005
Pro Thr Leu Lys Glu Asn Phe Arg Phe His Ala Ile Asn Gly Tyr Val
    1010   1015   1020
Lys Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln Lys Val Arg
1025   1030   1035   1040
Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His
                1045   1050   1055

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Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu Tyr Lys Met
        1060                1065                1070
Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu
        1075                1080                1085
Pro Ser Gln Val Gly Ile Trp Arg Ile Glu Cys Leu Ile Gly Glu His
    1090                1095                1100
Leu Gln Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Lys Lys Cys
1105                1110                1115                1120
Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile
                1125                1130                1135
Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu
        1140                1145                1150
His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Asp Pro Phe Ser
        1155                1160                1165
Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Met
    1170                1175                1180
Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Val Ser Gln Phe
1185                1190                1195                1200
Ile Ile Met Tyr Ser Leu Asp Gly Asn Lys Trp His Ser Tyr Arg Gly
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Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser
                1220                1225                1230
Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Gln Tyr Ile
        1235                1240                1245
Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu
    1250                1255                1260
Leu Leu Gly Cys Asp Phe Asn Ser Cys Ser Met Pro Leu Gly Met Glu
1265                1270                1275                1280
Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Leu Ser
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Ser Met Leu Ala Thr Trp Ser Pro Ser Gln Ala Arg Leu His Leu Gln
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Gly Arg Thr Asn Ala Trp Arg Pro Gln Ala Asn Asn Pro Lys Glu Trp
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Leu Gln Val Asp Phe Arg Lys Thr Met Lys Val Thr Gly Ile Thr Thr
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Gln Gly Val Lys Ser Leu Leu Ile Ser Met Tyr Val Lys Glu Phe Leu
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Ile Ser Ser Ser Gln Asp Gly His Asn Trp Thr Leu Phe Leu Gln Asn
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Gly Lys Val Lys Val Phe Gln Gly Asn Arg Asp Ser Ser Thr Pro Val
        1380                1385                1390
Arg Asn Arg Leu Glu Pro Pro Leu Val Ala Arg Tyr Val Arg Leu His
        1395                1400                1405
Pro Gln Ser Trp Ala His His Ile Ala Leu Arg Leu Glu Val Leu Gly
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23